

Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

## REMARKS

### Claim Status

Claims 1 - 46 are pending in the present application. No additional claims fee is believed to be due.

Claims 15 - 23 and 38 - 46 are canceled herewith without prejudice.

Applicants wish to thank the Examiner for rejoining of the methods claims of Groups I and III.

Independent claims 1, 8, 24, and 31 have been amended to spell out the term INGAP.

Claims 1 and 24 are also amended to replace "bound antibodies with a test sample" with "pre-attached antibodies with a test sample" to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Support for the amendment is found at page 3, lines 4 - 6 of the specification.

Claims 1, 2, 24, and 25 are also amended to replace "whereby INGAP protein in the test sample binds to the solid support" with "whereby INGAP molecule in the test sample binds to the antibodies and thereby to the solid support" to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Support for the amendment is found at page 3, lines 6 - 7 of the specification.

Claims 1 - 3, 7 - 10, 24 - 26, and 30 - 33 are also amended to replace the term "INGAP protein" with "INGAP molecule" to provide correct antecedent basis. Support for the amendment is found within claim 1 at line 7.

Claims 2 and 33 are amended to replace "the amount of marker protein" with "the amount of labeled INGAP molecule" to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Support for the amendment is found at page 10, Example 1 of the specification.

Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

It is believed these changes do not involve any introduction of new matter. Consequently, entry of these changes is believed to be in order and is respectfully requested.

Applicants also wish to draw attention to the change in Attorney Docket No. from 005126.00009 to 9056#LS.

Rejection under 35 USC §112, First Paragraph

The Office Action has rejected claims 24 – 37 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for residues 139 – 152 (SEQ ID NO: 3), and 151 – 164 (SEQ ID NO: 4); allegedly does not reasonably provide enablement for residues 104 – 118 (SEQ ID NO: 2). The Office Action further alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants respectfully disagree.

The Office Action cites two statements by Applicants in the specification. Applicants reproduce them below.

1. “that a peptide consisting of residues 104 – 118 (SEQ ID NO: 2) did not successfully compete with full length INGAP for binding to the antibodies” (Section 0017, Detailed Description of the Invention) (Emphasis in the Office Action).
2. “only INGAP 20 – 40 (SEQ ID NO: 1) functions in this assay” (Section 0056; Example 2, Figure 5) (Emphasis in the Office Action).

First, Applicants wish to draw attention to the preamble of claims 24 and 31, “A method for assaying islet neogenesis associated protein (INGAP) in a test sample”. Independent claims 24 and 31 (and also the dependent claims thereof) are directed towards methods of assaying INGAP molecule in a test sample that may contain INGAP, such as serum. Furthermore, the step (a) of both claims 24 and 31, state that a test sample is contacted with antibodies which specifically bind to an amino acid sequence selected

Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

from the group consisting of residues 104 – 118 (IGLHDPSHGTLPNGS; SEQ ID NO: 2), 139 – 152 (LAADRGYCAVLSQK; SEQ ID NO: 3), and 151 – 164 (QKSGFQKWRDFNCE; SEQ ID NO: 4) of INGAP molecule. Thus, the assays require antibodies that bind or recognize one particular epitope (as described by its amino acid positions in the INGAP molecule); however, these antibodies need not recognize every epitope on an INGAP molecule or every peptide that is derived from an INGAP molecule. In fact, it is normally observed, and may also be desired, that antibodies raised against a specific epitope do not cross-react with other unrelated epitopes. Thus, antibodies that are raised using the immunogen of SEQ ID NO: 2 would recognize the epitope of SEQ ID NO: 2 either on a peptide or in an INGAP molecule. However, these antibodies may not recognize the peptides of SEQ ID NOs: 1, 3 or 4. Applicants submit that in order to assay a test sample for the presence of INGAP molecule, antibodies raised against the peptide of SEQ ID NO: 2 are well suited.

Second, Applicants wish to point out that Section 0017 of the instant application describes data obtained using the peptide immunogen FLSWVEGEESQKKLPSSRITC (SEQ ID NO: 1) to raise the antibodies. Therefore, it is not untenable that peptide of SEQ ID NO: 2 was not able to displace the bound INGAP molecule from these antibodies. In fact, Applicants provide a cautionary note at page 6, lines 7 – 13:

Other peptide sequences can be used in place of residues 20 – 40 of INGAP.....Use of such peptides requires use of the corresponding antibody in the assay. (Emphasis added).

Similarly, it is not untenable that peptide of SEQ ID NO: 2 did not successfully compete in the assay depicted Figure 5. In fact, this inability of peptide of SEQ ID NO: 2 to compete with INGAP molecule in the displacement assay indicates that the antibodies are specific for the peptide of SEQ ID NO: 1. Again, Applicants wish to point to the Section titled "Brief Description of the Drawings, at page 3. The legend for Figure 5 reads:

Fig. 5 shows the specificity of the assay (Emphasis added). A peptide from a distinct region of INGAP (residues 104 – 118) was used as the tagged INGAP molecule. .

Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

In view of the above arguments, Applicants submit that claims 24 – 37 are enabled with respect to SEQ ID NO: 2. Applicants respectfully submit that the rejections based on 35 U.S.C. §112, first paragraph should be withdrawn.

Rejection under 35 USC §112, Second Paragraph

Claims 1 - 14 , and 24 – 37 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants submit that amended claims 1 – 14, and 24 – 37 particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Two of these rejections, not addressed by the present amendments are discussed below.

The Office Action states, “With respect to claim 1, lines 11 – 13, it is not clear why the labeled INGAP would bind to the solid support since the assay is based on competition where “unlabeled analyte (INGAP) in a sample competes with a labeled analyte for binding to the antibody (Section 0037).” Applicants respectfully disagree.

Claim 1 is directed to a method of assaying INGAP molecule in a test sample. However, the method of claim 1 is not directed to a competition assay. The INGAP molecules in the test sample are allowed to bind to the antibodies, and the unbound test sample is removed before the labeled INGAP molecules are provided to capture the remaining binding sites of the antibodies. The competitive assays that Section 0037 refers to are the methods of claim 8 and claim 31. Claims 8 and 31 are discussed further below.

The Office Action states, “With respect to claim 8 (and claim 31), it is not clear whether a separation step is required. If claim does not need a separation step, then how can one determine the reduction of the label(ed) due to competition”.

Claims 8 and 31 relate to methods for assaying INGAP molecule using competitive assays. As is explained in Section 0037, the unlabeled analyte (INGAP

Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

molecule) in a test sample competes with a labeled analyte for binding to an antibody that is labeled with a suitable complementary label. After incubation to achieve binding equilibrium, methods such as Fluorescent Resonance Energy Transfer (FRET) are used to determine the energy transfer between labeled analyte and labeled antibody. Use of FRET and other energy transfer techniques are within the scope of one skilled in the art. See Mikola, H, et al. (1995). "Syntheses and properties of luminescent lanthanide chelate labels and labeled haptenic antigens for homogeneous immunoassays." Bioconjug Chem 6(3): 235-41. Thus, Applicants submit that a separation step is not required for the methods of claims 8 and 31. Therefore, Applicants submit that both claims 8 and 31 are not indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, and the rejection based on 35 U.S.C. §112, second paragraph should be withdrawn.

#### Allowable Subject Matter

The Office Action has objected to claims 1 – 14 and 24 – 37 as allegedly being dependent upon a rejected based claim. The Office Action further suggests that these claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

It is unclear to Applicants how the claims could be rejected under various U.S.C. §112 provisions and also be allowable at the same time. Applicants request the Office to clarify its position.

Separately, Applicants have presently amended the claims. Applicants submit that the amended claims obviate the rejections and overcome the objections raised in the Office Action.


Appl. No. 10/036,418  
Atty. Docket No. 9056#LS  
Amdt. Dated 22 March 2005  
Reply to Office Action of 29 December 2004  
Customer No. 27752

Conclusion

In light of the above remarks, it is requested that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, first and second paragraph. Early and favorable action in the case is respectfully requested.

Respectfully Submitted,

THE PROCTER & GAMBLE COMPANY

By   
Naishadh N. Desai, Ph.D.  
Registration No. 50,630  
(513) 622 0087

Date: 22 March 2005  
Customer No. 27752  
9056\_Res\_First\_OA\_29March2005